REMARKS

Claims 1, 3, 35-58 are pending in the present application. New claim 58 is added. Claims 2 and 4-34 have been cancelled without prejudice or disclaimer. Claims 1, 3, 37, 38, 46, 47, 49 and 55-57 are amended. Basis for claim 58 can be found in the application on pages 12-13, lines 23-2. No new matter is added.

REJECTION OF CLAIMS UNDER 35 U.S.C. §112, First paragraph

1. Claims 1, 3 and 35-37

Claims 1, 3 and 35-37 are rejected under 35 U.S.C. § 112, first paragraph, as failing to comply with the written description requirement. It is alleged that the recitation "a membrane-bound protein having a plurality of helical regions" does not have basis in the instant specification.

Without agreeing to the propriety of the rejection, applicant has amended the claims to recite "a membrane-bound protein having a plurality of α helical regions." The amendment finds basis in the specification and claims as originally filed. Reconsideration and withdrawal of the rejection is requested.

2. Claims 1, 3, 37-39 and 41

Claims 1, 3, 37-39 and 41 are rejected under 35 U.S.C. § 112, first paragraph, for allegedly containing new matter. It is alleged that the recitation of "identifying two or more ranges of amino acids in the amino acid sequence" does not have basis in the application.

Applicant respectfully submits that the claims are amended to recite "identifying a range of amino acids in the amino acid sequence." The recitation finds basis in the application on pages 12-13, lines 23-2, which recite:

> The output from this step is a range or ranges of amino acids in the sequence that are predicted to be in the transmembrane region.

Reconsideration and withdrawal of the rejection is requested.

3. Claim 46

The limitation "effect of the environment of the membrane-bound protein" is allegedly not supported by the disclosure.

Applicant respectfully submits that claim 46 is amended to recite:

> The method of claim 1, wherein:
> optimizing a helix bundle configuration for the set of helices includes modeling an effect of an environment of the membrane-bound protein, wherein the effect of the environment is

simulated with a continuum description of a water environment and a lipid bilayer.

The amendment finds basis in the application on page 14, lines 6-9. Reconsideration and withdrawal of the rejection is requested.

4. Rejection of claims 56 and 57

The Office Action alleges that the limitations "four or more helices" in claim 56, and "seven or more helices" in claim 57, respectively, are not supported by the specification.

Applicant submits that Claim 56 is amended to specify that the four or more helices are membrane-spanning α helices. Claim 57 is amended to specify "seven membrane-spanning α helices." Basis for the amendment is found in the specification on page 19, lines 3-7.

REJECTION OF CLAIMS UNDER 35 U.S.C. §112, Second paragraph

Claims 47 and 49 are rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The Office Action alleges that the limitation "charges for the transmembrane protein" causes the claim to be vague and indefinite.

Applicant respectfully submits that claims 47 and 49 are amended to recite "membrane-bound protein." Reconsideration and removal of the rejection is requested.

REJECTION OF CLAIMS 1, 36-38, 41, 42, 44-46, 48, and 51-57 UNDER 35 U.S.C. §102(b)

Claims 1, 36-38, 41, 42, 44-46, 48, and 51-57 are rejected under 35 U.S.C. § 102(b) as anticipated by Biggins *et al.* It is alleged in the Office Action that Biggins *et al.* anticipates claims 1, 36-38, 41, 42, 44-46, 48, and 51-57 because it discloses computer method simulations predicting membrane bound proteins containing a plurality of α helix. The Office Action alleges that the reference provides amino acid sequences for the membrane-bound proteins wherein bacteriorhodopsin has, as set, 7 helices containing transmembrane regions. It is further alleged that Biggins *et al.* discloses using mean-field membrane simulations to provide a useful means to obtain information about possible conformations and/or orientations of a protein. The reference allegedly discloses that TM helix bundle models may be constructed by less costly simulations without bilayer, then refined (optimize) by subsequent (second simulation etc.) MD simulations in an atomistic bilayer or bilayers-mimetic environment. The Office Action urges that the reference

discloses the predicted structure outputted based on the all atom simulations. It is further alleged that Biggins discloses limitations of dependent claims 36, 38, 41, 42, 44, 45, 46, 48 and 51-57. Applicant respectfully disagrees.

The Instant claims

Applicant submits that instant claim 1 is directed to a computer implemented method for predicting the structure of a membrane-bound protein having a plurality of α-helical regions. The claimed method includes the steps of providing an amino acid sequence for the membrane-bound protein; identifying a range of amino acids in the amino acid sequence as transmembrane regions of the membrane-bound protein; constructing each of two or more helices in a set of helices for the transmembrane regions; optimizing a helix bundle configuration for the set of helices using a first molecular dynamics simulation; after optimizing the helix bundle configuration, constructing one or more inter-helical loops to generate a full-atom model of the membrane-bound protein; optimizing the full-atom model using a second molecular dynamics simulation; and outputting a predicted structure for the membrane-bound protein based on the second optimization. Claims 36-38, 41, 42, 44-46, 48, and 51-57 depend from claim 1 and further define the method.

The disclosure of Biggins *et al*.

The cited reference by Biggins *et al*. is a review article describing computer simulation studies of helix/bilayers interactions (see abstract and page 162). The reference describes various simulation studies of the interaction peptides and proteins with lipid bilayers, including mean-field simulations of helix-bilayer interaction. The reference also describes all atom simulations of helix-bilayer interaction. The reference discloses that mean-field simulations may play a role in generating initial configurations for subsequent atomistic simulations of helix-bilayer interaction. The reference does not disclose a method for predicting the structure of a membrane-bound protein having a plurality of α-helical regions.

Differences between claim 1 and the disclosure of Biggins et al.

As discussed above the cited reference discloses computer simulation studies of helix/bilayers interactions. The instant claim is directed to a method for predicting the structure of a membrane-bound protein having a plurality of α-helical regions. The claimed method includes providing an amino acid sequence for

the membrane-bound protein; identifying a range of amino acids in the amino acid sequence as transmembrane regions of the membrane-bound protein; constructing each of two or more helices in a set of helices for the transmembrane regions; optimizing a helix bundle configuration for the set of helices using a first molecular dynamics simulation; after optimizing the helix bundle configuration, constructing one or more inter-helical loops to generate a full-atom model of the membrane-bound protein; optimizing the full-atom model using a second molecular dynamics simulation; and outputting a predicted structure for the membrane-bound protein based on the second optimization.

Applicant respectfully submits that anticipation requires the disclosure in a single prior art reference of each element of the claim under consideration. In this case, the cited reference describes computer simulation studies of helix/bilayers interactions. It does not disclose a method for predicting the structure of a membrane-bound protein having a plurality of α-helical regions including the steps recited therein. Therefore, Biggins *et al.* does not anticipate the method of claim 1.

Because claims 36-38, 41, 42, 44-46, 48, and 51-57 depend from claim 1 and further define the method of claim 1, Biggins

et al. does not anticipate any of the rejected claims. Applicant respectfully requests that the rejection be reconsidered and withdrawn.

REJECTION OF CLAIMS 1, 3, 35-38, 41, 42, 44-46, 48, and 51-57 UNDER 35 U.S.C. §103(a)

Claims 1, 3, 35-38, 41, 42, 44-46, 48, and 51-57 are rejected under 35 U.S.C. 103(a) as being unpatentable over Biggin *et al*. taken with Rose *et al*. (U.S. Patent No. 5,680,319). Claims 1, 36-42, 44-46, 48-57 are further rejected under 35 U.S.C. 103(a) as being unpatentable over Biggin *et al*. taken with Mathiowetz *et al*. The Office Action rejects claims 1, 36-38, 41, 42, 44-48 and 50-57 under 35 U.S.C. 103(a) as being unpatentable over Biggin *et al*. taken with Mayo *et al*. Applicant disagrees.

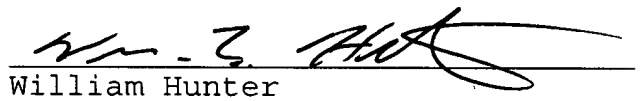
The allegation of obviousness of the rejected claims is based on the premise that Biggin *et al*. discloses the method of rejected claims. As discussed above, Biggin *et al*. describes computer simulation studies of helix/bilayers interactions. It does not provide any guidance for the method directed to predicting the structure of a membrane-bound protein having a plurality of α-helical regions including the steps recited therein as described in claim 1 and the claims dependent

thereon. None of the secondary references, remedy the deficiencies of Biggin *et al*. No further argument based upon the additionally cited references is needed. Accordingly, applicant requests reconsideration and withdrawal of the rejections.

Enclosed is a check in the amount of $510 to cover the fee for a three month extension of time. Please apply any other charges or credits to deposit account 06-1050.

Respectfully submitted,

Date: July 13, 2005



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